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Purpose/Objective: This analysis aimed to assess correlations between the most relevant acute toxicities (tox) and dosimetric risk factors during radiotherapy (RT) for nasopharyngeal cancer (NPC) and to identify patients (pts) suitable for studies on genetic determinants of radioinduced toxicity.
Materials and Methods: Since 2004, 156 consecutive NPC pts, with stages III-IV, received curative Intensity Modulated Radiation Therapy (IMRT) with or without chemotherapy (CHT) at a median total dose of 70 Gy with standard fractionation (2 Gy/fr). Planning data were collected and analyzed with a dedicated program (VODCA, www.vodca.ch). Acute mucositis, dysphagia and xerostomia were assessed according to Common Terminology Criteria for Adverse Events (CTCAE v4.0) at baseline and weekly during RT. Endpoints of this preliminary analysis were mean grade of mucositis ≥ 1.3, grade 3 dysphagia and grade 2 xerostomia recorded during RT. The Organs At Risk (OAR) selected as the most involved were oral cavity (OC) for mucositis; OC, pharyngeal constrictor muscles (PCM) and supraglottic larynx (SL) for dysphagia and OC and parotid glands for xerostomia. For those OARs, average DVHs of pts with/without each toxicity endpoint were compared through two-sided t-tests to assess the most discriminative values, according to the lowest p-values. Logistic uni- and multi-variate (MVA) analysis were performed, including selected dosimetric and clinical variables: a backward feature selection method based on prediction optimization (minimization of residual) was implemented in the KNIME (www.knime.com) environment. Residuals were used to identify the subpopulation to be selected for future genetic studies (i.e. pts with higher/lower toxicity with respect to the MVA prediction).
Results: Complete dosimetric data were available for 128 pts. Mean grade mucositis ≥ 1.3 was reported in 43 pts (32%), grade ≥ 3 dysphagia in 49 pts (37%) and grade ≥ 2 xerostomia in 89 pts (67%). MVA resulted in a single variable model - OC V62.5Gy - for mucositis (OR=1.04, p=0.004); a 3-variable model for dysphagia including OC V62.5Gy (OR=1.03, p=0.05), minimum dose to PCM (OR=1.06, p=0.05) and SL V30Gy (OR=1.05, p=0.37); a 2-variable model for xerostomia including parotid glands V72.5Gy (OR=1.09, p=0.21) and OC V65Gy (OR=1.06, p=0.01). Calibration was good in all cases. Calculation of residuals allowed the identification of high-residual pts, 15 (12%) for mucositis and 9 (7%) for dysphagia, who exhibited toxicity despite their low MVA prediction suggesting a potential radiosensitivity. Conversely, 9 (7%) low-residual pts for xerostomia who did not exhibit toxicity despite their high MVA prediction might imply a potential radioresistance.
Conclusions: Preliminary analysis suggests a dose-response relationship for acute mucositis, dysphagia and xerostomia. Residual pts with respect to dosimetric models were identified and could be good candidates for analysis of genetic determinants of radioinduced toxicity.

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Commissioning radiobiological metrics for 3D patient-specific quality assurance

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Purpose/Objective: The patient-specific QA programs have evolved substantially during the last years. The transition from point and 2D verifications to 3D verifications on patient anatomy is being carried out. This information allows to introduce DVH-based metrics in QA process. In addition, the quality of a RT plan can be judged by radiobiological parameters. This work shows the clinical introduction of radiobiological metrics (gEUD, TCP and NTCP) in patient-specific QA by means of a benchmark test described in the AAPM report of the Task Group 166.
Materials and Methods: The Compass system is capable to calculate and reconstruct dose on patient anatomy. In order to evaluate the introduction of radiobiological metrics in patient-specific QA process, a simple plan test was performed using a benchmark case taken from AAPM TG-166 report. This case consisted on a single 6 MV, 20 x 20 cm^2 photon beam incident on a cubic and homogeneous phantom at 100 cm SSD, with four simple structures (three rectangular, one triangular) defined in the report. A dose of 72 Gy in 40 fractions was prescribed to a point at 6 cm depth along the central axis. This plan was generated by the TPS (Monaco 3.1, Elekta) and delivered in the treatment unit (Synergy, Elekta). During this delivery, beam was measured by the Compass system. It provided the redundant calculation and the dose reconstruction from measurements over the TG-166 structures contoured on benchmark phantom. gEUD, TCP (Poisson, Sigmoidal and Niermierko models) and NTCP (LKB and Niermierko models) were determined for the previous structures, from the TPS, Compass calculated and Compass reconstructed data.
Results: The relative mean differences for all structures between Compass and TPS for gEUD parameter were (0.25±0.78)% and (0.24±0.77)% for Compass dose calculation and reconstruction results, respectively. The mean differences for the TCP models (Poisson, Sigmoidal and Niemierko, respectively) were (-0.24±0.33)%, (-0.18±0.33)% and (-0.19±0.26)% for the Compass dose calculation results, and (0.34±0.53)%, (0.18±0.34)% and (0.16±0.24)% for the Compass dose reconstruction results. For the NTCP models (LKB and Niemierko, respectively), the mean discrepancies were (-0.13±0.72)% and (0.37±0.60)% for the Compass dose calculation results and (0.30±0.85)% and (-0.19±0.77)% for the Compass dose reconstruction results.
Conclusions: Mean discrepancies were below 1% for all the radiobiological parameters analyzed in this benchmark case. Radiobiological parameters are powerful evaluation tools for radiation therapy treatment plans. 3D dose verification systems allow to introduce radiobiological data in the patient-specific QA process, as an additional metric in a pretreatment verification program.